Aggressive B-cell Lymphoma
Diagnostic Algorithm

**PATHC / Pathology Consultation**
The final diagnosis requires 4 components:
- Morphologic diagnosis: HGBCL vs DLBCL
- COO (per Hans algorithm): Germinal center B-cell phenotype vs non-germinal center B-cell phenotype
- BCL2/MYC expression: Double expressor vs non-double expressor
- FISH result: presence vs absence of MYC and BCL2 and/or BCL6 rearrangements

**Morphology: DLBCL, HGBCL, or Burkitt lymphoma**

- Positive for MYC rearrangement
  - FISH: BCL2 and BCL6 BAP
  - IGH/MYC, IGK/MYC, IGL/MYC D-FISH
  - Negative for BCL2 and/or BCL6 rearrangements
    - Morphology: DLBCL vs HGBCL vs Burkitt lymphoma
      - HGBCL vs Burkitt lymphoma
      - IHC: CD10, CD43, BCL2, BCL6, MUM1, MYC
        - CD10+, CD43+, BCL6+, MUM1-, MYC+, BCL2–: Probably Burkitt lymphoma, confirm with morphology and clinical
        - HGBCL, not otherwise specified

- Negative for MYC rearrangement
  - Morphology: DLBCL vs HGBCL
  - Burkitt lymphoma likely excluded, however:
    - Consider CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded for 11q23 aberrancy and 11q24-ter deletion
    - Consider D-FISH for IGH/MYC, IGK/MYC, and IGL/MYC to completely exclude a MYC rearrangement

**BLYMF / B-Cell Lymphoma, FISH, Tissue**

- MYC BAP probe
  - CD10+, CD43+, BCL6+, MUM1–, MYC+, BCL2–: Probably Burkitt lymphoma, confirm with morphology and clinical
  - HGBCL, not otherwise specified

**COO IHC (CD10, BCL6, MUM1) and double expressor IHC (BCL2 and MYC)**

- BCL2+ and MYC+ (Double expressor)
  - Hans IHC: CD10
    - **POSITIVE**
      - Germinal center B-cell phenotype
    - **NEGATIVE**
      - BCL6
        - **POSITIVE**
          - MUM1
            - **POSITIVE**
              - Non-germinal center B-cell phenotype
            - **NEGATIVE**
              - Germinal center B-cell phenotype
        - **NEGATIVE**
          - Not a double expressor

- BCL2+ and MYC+ (Double expressor)
  - Hans IHC: CD10
    - **POSITIVE**
      - Germinal center B-cell phenotype
    - **NEGATIVE**
      - BCL6
        - **POSITIVE**
          - MUM1
            - **POSITIVE**
              - Non-germinal center B-cell phenotype
            - **NEGATIVE**
              - Germinal center B-cell phenotype
        - **NEGATIVE**
          - Not a double expressor